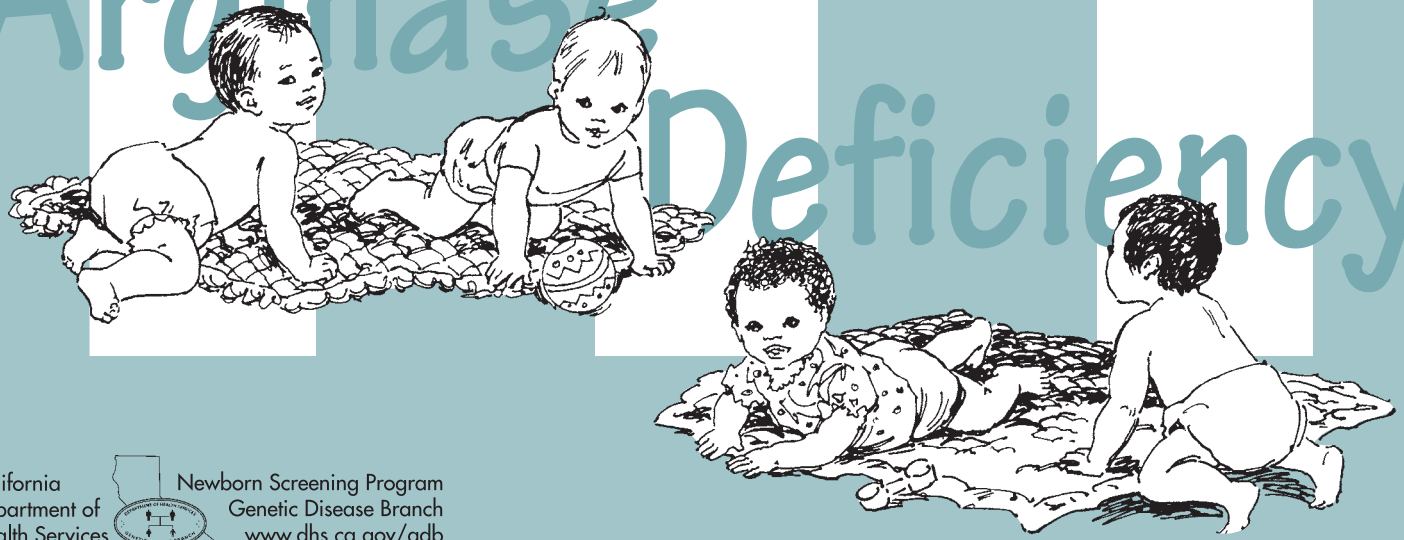
Parents' Guide to Arginase Deficiency



California
Department of
Health Services

Newborn Screening Program
Genetic Disease Branch
www.dhs.ca.gov/gdb

June 2005

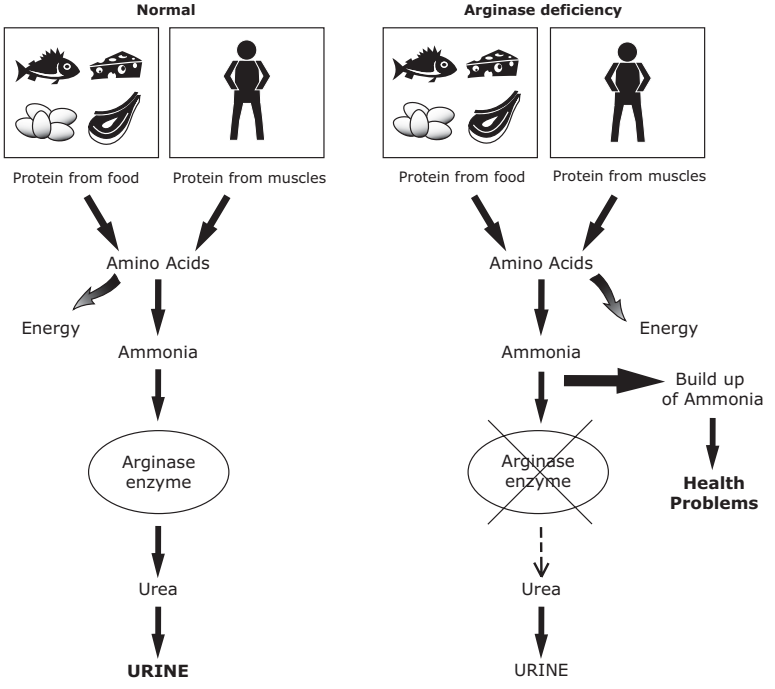
Table of Contents

The information in this booklet is general and is not meant to be specific to each child with arginase deficiency. Certain treatments may be recommended for some children but not others. Children with arginase deficiency should be followed by a physician specializing in metabolic diseases (metabolic specialist) in addition to their primary doctor. For a list of metabolic centers, see page 18 or visit our website at www.dhs.ca.gov/gdb.

*Underlined words in booklet are defined in the Glossary

What is arginase deficiency?

Arginase deficiency is one type of amino acid disorder. People with this condition have problems removing ammonia from the body. Ammonia is a harmful substance. It is made when protein and its building blocks, amino acids, are broken down for use by the body.



What causes arginase deficiency?

This is one of a small number of amino acid disorders called "urea cycle disorders" (UCD).

It occurs when an enzyme called "arginase" is either missing or not working properly. This enzyme's job is to help break down the amino acid arginine and to help remove ammonia from the body.

When arginase is not working, arginine, along with ammonia, can build up in the blood. This can cause serious effects on growth, learning and health.

What causes the arginase enzyme to be missing or not working correctly?

Genes tell the body to make various enzymes. People with arginase deficiency have a pair of genes that do not work correctly.

Because of the changes in this pair of genes, the arginase enzyme either does not work properly or is not made at all.

If arginase deficiency is not treated, what problems occur?

The effects of this condition vary from person to person.
Symptoms can start right at birth or not until later in childhood.
Many children have their first symptoms around one year of age.
Effects in infants can include:

- poor growth
- learning delays
- spasticity
- poor coordination and balance problems
- fussiness or illness when fed high protein food

Episodes of illness caused by high ammonia levels in the blood can sometimes occur but are not common. Some of the first symptoms of high ammonia are:

- poor appetite
- excess sleepiness or lack of energy
- irritability
- vomiting

If untreated, other symptoms can follow:

- muscle weakness
- decreased or increased muscle tone
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, and sometimes death

Sometimes, symptoms of arginase deficiency do not begin until later in infancy or childhood. Common effects in older infants and children include:

- poor growth
- spasticity
- small head size
- hyperactivity
- behavior problems
- learning disabilities
- avoidance of meat or other high protein foods
- occasional bouts of vomiting and excessive sleepiness

Episodes of high ammonia, described above, happen rarely. If they occur, they are more likely to happen:

- after going without food for long periods
- during illness or infection
- after high-protein meals

What happens when arginase deficiency is treated?

With prompt and lifelong treatment, children with arginase deficiency may be able to live healthy lives with typical growth and learning.

Even with treatment, some children still have effects from high blood levels of arginine and ammonia. This can result in permanent learning problems, mental retardation or spasticity.

What is the treatment for arginase deficiency?

Your baby's primary doctor will work with a metabolic specialist and a dietician to care for your child.

Prompt treatment is needed to prevent the build-up of arginine and ammonia. You should start treatment as soon as you know your child has the condition.

The following treatments are often recommended for babies and children with arginase deficiency:

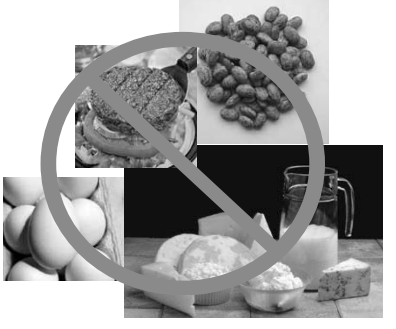
1. Low-protein diet and/or special medical foods and formula

Most children need to eat a diet made up of very low-protein foods and special medical foods. Your dietician will create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. The food plan should be continued throughout your child's life.

Low-protein diet

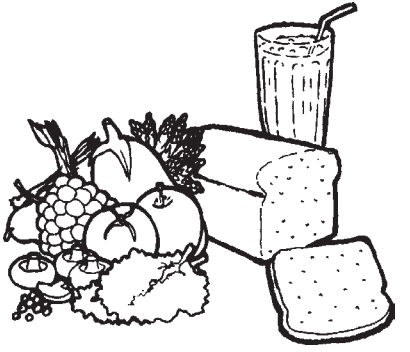
One of the main treatments is a low-protein diet. Foods that need to be avoided or limited include:

- milk, cheese and other dairy products
- meat and poultry
- fish
- eggs
- dried beans and legumes
- nuts and peanut butter



Eating these foods can cause ammonia and arginine to build up, resulting in the symptoms described above. Many vegetables and fruits have only small amounts of protein and can be eaten in carefully measured amounts.

Do not remove all protein from the diet. Your child still needs a certain amount of protein for normal growth and development. Any changes in the diet should be made under the guidance of a dietician.



Medical foods and formula

There are medical foods such as special low-protein flours, pastas, and rice that are made especially for people with amino acid disorders.

Your child may be given a special formula that contains the correct amount of nutrients and amino acids. Your metabolic specialist and dietician will tell you whether your child should use this formula and how much to use.

Your child's exact food plan will depend on many things such as his or her age, weight, and general health. Your dietician will fine-tune your child's diet over time.

2. Medication

There are certain medications that can help the body get rid of excess arginine and ammonia. Your metabolic specialist will decide which medications your child should take.

3. Blood tests

Your child will need to have regular blood tests to measure ammonia and amino acid levels. Your child's diet and medication may need to be adjusted based on blood test results.

4. Call your doctor immediately at the sign of symptoms in your child:

Illness or infection can sometimes lead to high arginine and ammonia levels. In order to prevent problems, call your doctor right away when your child has any of the following:

- loss of appetite
- low energy or excessive sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes
- difficulty walking or balance problems

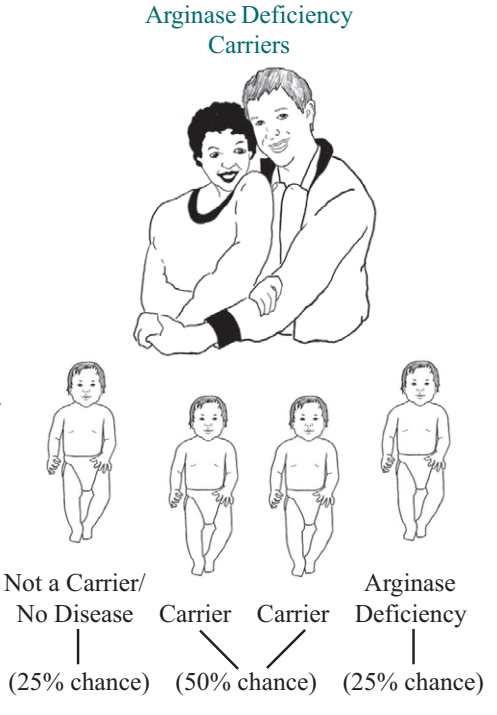
How is arginase deficiency inherited?

Arginase deficiency affects both boys and girls equally.

Everyone has a pair of genes that make the arginase enzyme. In children with arginase deficiency, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent. This is called autosomal recessive inheritance.

Parents of children with arginase deficiency rarely have the condition themselves. Instead, each parent has a single non-working gene for the condition. They are called carriers. Carriers are not affected because their other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have two working genes. This means the child is not a carrier and does not have the disease. There is a 50% chance for the child to be a carrier, just like the parents. There is a 25% chance for the child to have arginase deficiency.



Genetic counseling is available to families who have children with this condition. Genetic counselors can answer your questions about how arginase deficiency is inherited, options during future pregnancies, and how to test other family members. Other family members can also ask about genetic counseling and testing for arginase deficiency.

Is genetic testing available?

Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause the condition. Talk with your genetic counselor or metabolic specialist about whether DNA testing is possible for your family.

DNA testing may not be necessary to diagnose your child. However, it can be helpful for carrier testing or prenatal diagnosis.

What other testing is available?

Special blood and urine tests can be done to confirm arginase deficiency. Talk to your metabolic specialist or genetic counselor if you have questions about diagnostic testing.

Can you test during pregnancy?

DNA testing may be possible during future pregnancies. The sample needed for DNA testing is obtained by either CVS or amniocentesis.

If DNA testing is not available, an enzyme test may be done using a blood sample from the fetus. The sample needed is obtained by a procedure called fetal blood sampling.

Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have arginase deficiency or be carriers?

If they are healthy and growing normally, older brothers and sisters of a baby with arginase deficiency are at low risk of having the condition. However, finding out whether other children in the family have the condition may be important because early treatment can prevent serious health problems. Ask your metabolic specialist whether your other children should be tested.

Brothers and sisters who do not have arginase deficiency still have a chance to be carriers like their parents. Carriers do not have the disorder and will never develop it.

Each of the parents' brothers and sisters has a chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with arginase deficiency.

When both parents are known arginase deficiency carriers or have had a baby with arginase deficiency, subsequent newborns should have special diagnostic testing in addition to the newborn screen to test for arginase deficiency.

How many people have arginase deficiency?

About one in every 300,000 babies in the United States is born with this condition.

Does arginase deficiency happen more frequently in a certain ethnic group?

Arginase deficiency does not appear to happen more often in any specific race, ethnic group, geographical area or country.

Does arginase deficiency go by any other names?

Arginase deficiency is sometimes also called:

- argininemia
- hyperargininemia

RESOURCES

National Urea Cycle Disorders Foundation
4841 Hill St.
La Canada, CA 91011
www.nucdf.org

Children Living with Inherited Metabolic Disorders
CLIMB Building
176 Nantwich Road
Crewe, CW2 6BG
United Kingdom
www.climb.org.uk

National Coalition for PKU and Allied Disorders
PO Box 1244
Mansfield, MA 02048
www.pku-allieddisorders.org

Genetic Alliance
4301 Connecticut Ave. NW, Suite 404
Washington, DC 20008-2369
(202) 966-5557
www.geneticalliance.org

CALIFORNIA METABOLIC CENTERS

Cedars-Sinai Medical
Center, Los Angeles
(310) 423-9914

Children's Hospital Central
California, Madera
(559) 353-6400

Children's Hospital &
Research Center, Oakland
(510) 428-3550

Children's Hospital
Los Angeles
(323) 660-2450

Children's Hospital of
Orange County, Orange
(714) 532-8852

Children's Hospital and
Health Center of San Diego
(619) 543-7800

Harbor/UCLA Medical Center
Torrance
(310) 222-3756

Kaiser Permanente - No. Cal.
(510) 752-7703

Kaiser Permanente - So. Cal.
(323) 783-6970

LAC/USC Medical Center
Los Angeles
(323) 226-3816

Lucile Salter Packard Children's
Hospital at Stanford
(650) 723-6858

Sutter Medical Center
Sacramento
(916) 733-6023

UC Davis Medical Center
(916) 734-3112

UC San Francisco Medical Center
(415) 476-2757

UCLA Medical Center
(310) 206-6581

UCI Medical Center, Orange
(714) 456-8513

GLOSSARY

Amino acid disorders - A group of rare inherited conditions. People with amino acid disorders cannot digest particular amino acids – the building blocks of protein. These amino acids, along with other toxic substances, build up in the body. This can cause serious effects on health, growth, and learning.

Ammonia - A waste product made when protein is broken down for the body to use. Ammonia is harmful to the body. It is usually changed to a harmless substance called “urea”. Urea is then removed from the body in the urine. People with urea cycle disorders cannot get rid of ammonia. If these conditions are not treated, ammonia can build up and cause serious health problems.

Amniocentesis - Test done during pregnancy (usually between 16 and 20 weeks). A needle is used to remove a small sample of fluid from the sac around the fetus. The sample can be used to test for certain genetic disorders in the fetus.

Arginine - One of 20 amino acids that make up protein. It is also known as “Arg”. Most of the arginine needed is made by the body. In most cases, it does not need to be eaten in the diet. Arginine can also be bought in pill form. Children with

certain urea cycle disorders are often given arginine supplements. These supplements can help clear the body of ammonia.

Autosomal recessive - Autosomal recessive conditions affect both boys and girls equally. How autosomal recessive inheritance works: Everyone has a pair of genes responsible for making each enzyme in the body. A person with a metabolic disorder has one enzyme that is either missing or not working properly. The problem is caused by a pair of "recessive" genes that are not working correctly. They do not make the needed enzyme. A person has to have two non-working "recessive" genes in order to have an autosomal recessive metabolic disorder. A person with an autosomal recessive disorder inherits one non-working gene from their mother and the other from their father.

Carrier - A person who has a gene mutation in one of their genes that causes a disease, but does not have any symptoms of the disease. The mutation is often recessive, which means that both copies of the gene have to be mutated in order for disease symptoms to develop. Carriers are able to pass the mutation onto their children and therefore have an increased chance of having a child with the disease.

CVS - Chorionic Villus Sampling (CVS) is a special test done during early pregnancy (usually between 10 and 12 weeks). A small sample of the placenta is removed for testing. This sample can be used to test for certain genetic disorders in the fetus.

DNA - Deoxyribonucleic acid (DNA) is a molecule that makes up chromosomes. It is composed of four units (called bases) that are designated A, T, G, and C. The sequence of the bases spell out instructions for making all of the proteins in an organism. The instructions set for each individual protein is a gene. A change in one of the DNA letters making up a gene is a mutation. In some cases, these mutations can alter the protein instructions and lead to disease. Each individual passes their chromosomes on to their children, and therefore passes down the DNA instructions. It is these instructions that cause certain traits, such as eye or hair color, to be inherited.

Enzyme - A molecule that helps chemical reactions take place. For example, enzymes in the stomach speed up the process of breaking down food. Each enzyme can participate in many chemical reactions without changing or being used up.

Fetal blood sampling - A special test done during pregnancy. A needle is used to remove a small amount of blood from the umbilical cord of the fetus. This blood sample can be used to test for certain genetic disorders in the fetus. Fetal blood sampling, also called PUBS, is usually done between 18 and 23 weeks of pregnancy.

Gene - A segment of DNA that contains the instructions to make a specific protein (or part of a protein). Genes are contained on chromosomes. Chromosomes, and the genes on those chromosomes, are passed on from parent to child. Errors in the DNA that make up a gene are called mutations and can lead to diseases.

Genetic Counseling - Genetic counseling gives patients and their families education and information about genetic-related conditions and helps them make informed decisions. It is often provided by Genetic Counselors or Medical Geneticists who have special training in inherited disorders.

Muscle tone - In order to hold our posture and control our movements, a certain amount of tension is needed in our muscles. This tension is call “muscle tone”. People with hypotonia have too little tension in their muscles and appear “floppy”. People with hypertonia have too much tension in their muscles and have problems

with tight, rigid muscles and joints.

Seizure - Also called “convulsions” or “fits.” During a seizure, a person may lose consciousness and control of their muscles. It may also cause involuntary movements. Seizures can happen for many reasons. Some causes are metabolic disorders, a metabolic crisis, brain injury, and infection.

Spasticity - Rigidity of the muscles and increased reflexes. It is caused by increased muscle tone. It results in abnormal tightness or stiffness of the muscles and joints.

Urea Cycle Disorders - Inherited conditions that cause ammonia to build up in the body. Ammonia is a harmful waste product made during the breakdown of protein and its amino acid building blocks.

NOTES OR QUESTIONS FOR MY DOCTOR

This booklet has been adapted from the materials developed by STAR-G Project — a multi-state collaborative project including representatives from California DHS, Newborn Screening Program, and funded by a federal grant from the MCH Bureau, Project #1 H46 MC 00189-02.

Acknowledgements

We would like to thank the following people for their help in reviewing and providing input into this booklet:

- Metabolic Specialists and Dieticians at California Children's Services (CCS) Approved Metabolic Centers
- California Newborn Screening Area Service Center staff
- Parents of children with Arginase Deficiency